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OFFICE OF THE PRESIDENT

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Dear Jim: Darnell

WHY INTRONS?

John Cairns' atrocious experiments totally lack persuasion; but they've led me to think more about the speculation of "environmental stress" leading to genetic instability -- a not implausible feedback, perhaps of limited specificity, -- a far cry from the lamarckian interpretations. See enclosed reprint (P27x).

In turn, that's led me to wonder if accumulated m-RNA might be a) mutagenic, b) interfere with DNA replication, or c) interfere with transcription, any of these by virtue of sequence homology with the genomic DNA. [Not to mention reverse transcription].

If so, then the excision of introns might serve the function of reducing that DNA=RNA homology on the part of completed transcripts.

This should be susceptible to experimental test. What (besides issues related to the versatility of alternative splicings) is known about the functional consequences of replacing a gene with its corresponding c-DNA?

Has this hypothesis been discussed before?

Yours sincerely,

Joshua

Joshua Lederberg

P.S. some additional references.

Davis, B.D. 1989 PNAS 86: 5005 (on transcriptional bias).

Drake, JW 1989 Env. Mol. Mut. 14: (S16): 11-15. — good general review of mutagenesis.

Hall, BG 1989. Genome 31: 265 Another case of "induced mutation.

Mellon, I. & Hanawalt, P. 1989. DNA repair and transcription. Nature 342: 95-98.

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